

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date
15 September 2005 (15.09.2005)

PCT

(10) International Publication Number
WO 2005/084190 A2

(51) International Patent Classification: Not classified

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(21) International Application Number:

PCT/US2005/003245

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(22) International Filing Date: 3 February 2005 (03.02.2005)

(25) Filing Language: English

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(26) Publication Language: English

(30) Priority Data:

60/542,780	5 February 2004 (05.02.2004)	US
60/556,831	26 March 2004 (26.03.2004)	US
60/575,919	1 June 2004 (01.06.2004)	US
10/912,932	6 August 2004 (06.08.2004)	US

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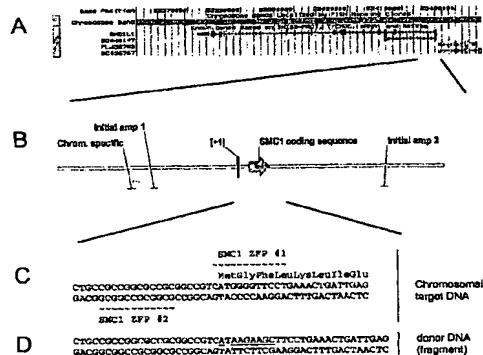
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(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: METHODS AND COMPOSITIONS FOR TARGETED CLEAVAGE AND RECOMBINATION



(57) Abstract: Disclosed herein are methods and compositions for targeted cleavage of a genomic sequence, targeted alteration of a genomic sequence, and targeted recombination between a genomic region and an exogenous polynucleotide homologous to the genomic region. The compositions include fusion proteins comprising a cleavage domain (or cleavage half-domain) and an engineered zinc finger domain, as well as polynucleotides encoding same. Fusion proteins comprising cleavage half-domains are used in pairs, to reconstitute a functional cleavage domain. In these fusion proteins, the zinc finger domain can be N-terminal to the cleavage half-domain, or the cleavage half-domain can be N-terminal to the zinc finger domain. The availability of fusion endonucleases having these different polarities allows targeting (and thereby binding) of zinc finger endonucleases either to opposite strands of the DNA target or to the same strand of the DNA target, thereby increasing the number of possible sequences which can be targeted and cleaved by the fusion proteins.

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Published:

— *without international search report and to be republished upon receipt of that report*

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